Translation

PCT/EP2003/002969

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 24991 WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP2003/002969	International filing date (*day/month/year*) 21 March 2003 (21.03.2003)	Priority date (*day/month/year*) 22 March 2002 (22.03.2002)
International Patent Classification (IPC) or national classification and IPC A61K 48/00		
Applicant ORTHOGEN AG		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18 July 2003 (18.07.2003)	23 March 2004 (23.03.2004)
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP2003/002969

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:

pages 1-40, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☒ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages 1-39, filed with the letter of 01 March 2004 (01.03.2004)

☒ the drawings:

pages 1/11-11/11, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP 03/02969

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2-4,6-18,21-29,31-39	YES
	Claims	1-5,19-20,30	NO
Inventive step (IS)	Claims	4,6	YES
	Claims	1-3,5,7-39	NO
Industrial applicability (IA)	Claims	1-39 (see below)	YES
	Claims		NO

2. Citations and explanations

D1: US-A-5 399 346 (ANDERSON W FRENCH ET AL) 21 March 1995 (1995-03-21)

D2: US 2002/034495 A1 (ANDERSON W FRENCH ET AL) 21 March 2002 (2002-03-21)

D3: WO 01 75131 A (UNIV TECHNOLOGY CORP) 11 October 2001 (2001-10-11)

*D4: Molecular Biotechnology 5(3), 259-261 (1996) Matthews & Keating

*D5: BioTechniques 17(6), 1118-1125 (1994) Clarke et al.

* These documents (not attached) are cited for the first time and were not mentioned in the international search report.

- *See the citations in the international search report.*

1. The wording of claim 1 is not clear, since the claim relates to more than just a method in which whole blood (cells) is (are) transformed without prior separation of (blood) cells.

Claim 5, which is dependent on claim 1, makes this clear, namely that claim 1 should also encompass

methods that are neither novel nor inventive, since they essentially cover only the isolation of blood cells and the subsequent transformation thereof (see page 2, second paragraph and D1 and D2: transfection of different blood cell fractions and types).

2. In this respect, page 6 makes clear in lines 14-17 the essence of the invention, namely that blood is transformed in such a manner that the blood cells to be transformed are *not* separated from the other blood components of the drawn blood beforehand, meaning that they are not fractioned.

Wording to this effect could redress the lack of clarity as to the scope of claim 1.

3. Methods for transforming cells using glass microbeads are known as one of the possible transformation processes, and therefore claims 19-20 and 30 lack novelty and claim 16 is not regarded as inventive (yeast: page 2, penultimate paragraph; mammalian cells: D4 and D5).

The blood cell transformation and the transformation of various types of blood cells are described in D1 and D2.

In light of the above, the transformation of blood cells using glass microbeads cannot be regarded as inventive.

Therefore, claims 1-3, 5, 7-15 and 17, 20-24 and 30-34 lack an inventive step.

4. Claims 25 and 35 lack clarity. What is the indicated

drug kit comprised of?

Furthermore, claims 25 and 35 are not inventive with respect to D1 and D2, which describe transformed blood cells for therapy.

Consequently, claims 25-29 and 35-39 cannot be regarded as inventive.

5. It should be noted therefore that simply identifying a successful therapeutic application ("therapeutic application... with the systems described here"; page 35) without indicating more precise measurement results or data is not sufficient for demonstrating that an inventive step is involved.

The applicant has substantially shown beyond a doubt that the transformation of whole blood using coated glass beads yields expression of the DNA used (cDNA for IL-1Ra) to form the corresponding IL-1 receptor antagonist protein IL-1ra, which is above the control values (figure 8, page 28; figure 9, page 34).

6. Claims 35-39 contain all of the essential features of claims 25-29. The same applies to claims 30-34 and 20-24.

In the interest of clarity and concision, the former group of claims in each case should not be independent claims, but rather should merely be worded as being dependent on the latter group of claims.

7. Claim 18 lacks clarity and should contain a

reference to a method which is described or to which reference is made in the claims.

8. The PCT Contracting States do not have uniform criteria for assessing the industrial applicability of present claim 17 in its present form. Patentability may also depend on the wording of the claims. The EPO, for example, does not recognise the industrial applicability of claims to the medical use of a compound; it may, however, allow claims to the first medical application of a known compound or to the use of such a compound in the manufacture of a drug for a new medical application.